THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALZA CORPORATION

Appeal No. 97-0383
Reexamination No. 90/003,535[1]

HEARD: September 17, 1997

Before McCANDLISH, Senior Administrative Patent Judge, STAAB and McQUADE, Administrative Patent Judges.

McCANDLISH, Administrative Patent Judge.

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[1] Reexamination request filed August 19, 1994. This Reexamination proceeding for U.S. Patent No. 5,232,438 issued August 3, 1993 is based upon application 07/898,618 filed June 15, 1992; which is a continuation of application 07/648,269 filed January 30, 1991, now U.S. Patent No. 5,169,382 issued December 8, 1992; which is a continuation of application 07/252,402 filed October 3, 1988, now U.S. Patent No. 5,080,646 issued January 14, 1992.

DECISION ON APPEAL

This is a decision on an appeal from the examiner's final rejection of claims 1 through 24 in the above-identified reexamination proceeding. No other claims are pending in this proceeding.

The claimed invention relates to the iontophoretic or electrotransport delivery of an analgesic drug transdermally through the intact skin of a living animal, the analgesic drug being selected from the group consisting of fentanyl, sufentanil, analogues of fentanyl, analogues of sufentanil and pharmaceutically acceptable salts thereof.

A copy of the appealed claims is appended to appellant's brief.

The following references are relied upon by the examiner as evidence of obviousness in support of his rejections under 35 U.S.C. § 103:

Ariura et al. (Ariura)	4,474,570	Oct. 2, 1984
Gale et al. (Gale)	4,588,580	May 13, 1986
Petelenz et al. (Petelenz)	4,752,285	Jun. 21, 1988
Sasaki	4,764,164	Aug. 16, 1988

Japanese patent (Yamanaka)[2] 62-135435 Jun. 18, 1987

Gatipon, “Morphine and Brain Stem Neurons: Microiontophoretic Study of Respnses to Noxious Stimulation in the Cat,” The Pharmacologist, Dept. of Pharmacology and Toxicology, Univ. Miss. Med. Ctr. (1976) p. 177.

Gangarosa et al. (Gangarosa), “Conductivity of Drugs Used for Iontophoresis,” Journal of Pharmaceutical Sciences, Vol. 67, No. 10 (October 1978) pp. 1439-1443.

Hewson et al. (Hewson), “The Effects of Anilidopiperidine Analgesics on Single Respiratory and Non-Respiratory Neurones in the Brain Stem of the Rat,” Life Science, Vol. 31 (1982) pp. 2335-2338.

Tyle, “Iontophoretic Devices for Drug Delivery,” Pharmaceutical Research, Vol. 3, No. 6 (1986) pp. 318-326.

Sebel et al. (Sebel), “Transdermal Absorption of Fentanyl and Sufentanil in Man,” European Journal of Clinical Pharmacology, Vol. 32 (1987) pp. 529-531.

Banga et al. (Banga), “Iontophoretic Delivery of Drugs: Fundamentals, Developments and Biomedical Applications,” Journal of Controlled Release, 7 (1988) pp. 1-24.

Stanley, “New Routes of Administration and New Delivery Systems of Anesthetics,” The Journal of Anesthesiology, Vol. 68, No. 5 (May 1988) pp. 665-668.

The grounds of rejection are as follows:

1. Claims 1 through 24 stand rejected under 35 U.S.C.

[2] Translation attached.

§ 103 as being unpatentable over Ariura in view of Gatipon or Hewson.

2. Claims 1 through 24 additionally stand rejected under 35 U.S.C. § 103 as being unpatentable over Ariura in view of Gale, Banga, Tyle, Gangarosa and Stanley.

3. Claims 1 through 24 also stand rejected under 35 U.S.C.
§ 103 as being unpatentable over Petelenz in view of Ariura and Gatipon.

4. Claims 1 through 24 also stand rejected under 35 U.S.C.
§ 103 as being unpatentable over Sebel in view of Tyle, Banga and Ariura.

5. Claims 1 through 24 also stand rejected under 35 U.S.C.
§ 103 as being unpatentable over Sasaki in view Yamanaka.

Reference is made to the examiner’s answer for details of these rejections.

Although we cannot agree with some of the contentions in appellant’s main brief, we nevertheless cannot sustain any of the examiner’s rejections of the appealed claims.

With regard to the rejection based on Ariura and Gatipon or Hewson, none of the references applied in this rejection teaches that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to transdermal delivery (i.e., delivery through the intact skin). Although Ariura teaches a device for iontophoretically delivering an analgesic drug transdermally through the intact skin, this reference contains no disclosure of fentanyl or any of the other drugs recited in the above-mentioned Markush group. On the other hand, both Gatipon and Hewson recognize that fentanyl has properties making it susceptible to iontophoretic delivery. However, neither of these references recognizes that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to transdermal delivery.

With regard to the rejection based the combined teachings of Ariura, Gale, Banga, Tyle, Gangarosa and Stanley, none of the references applied in this rejection teaches that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to iontophoretic delivery. As noted supra, Ariura contains no

disclosure of fentanyl or any of the other drugs recited in the above-mentioned Markush group. Gale and Stanley do recognize that fentanyl possesses properties making it susceptible to transdermal delivery. However, neither of these references recognize that fentanyl also possesses properties making it susceptible to iontophoretic delivery. Banga, Gangarosa and Tyle, on the other hand, all teach the concept of transdermally delivering anesthetic drugs, generally, by iontophoresis, but none of these references contains a disclosure of fentanyl or any of the other drugs recited in the above-mentioned Markush group.

With regard to the rejection based on the combined teachings of Petelenz, Ariura and Gatipon, none of the references applied in this rejection teaches that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to transdermal delivery. Petelenz does recognize that drugs, such as morphine, may be iontophoretically delivered transdermally through the skin. However, this reference, like Ariura, contains no disclosure of fentanyl or any of the other drugs recited in the above-mentioned Markush group. Gatipon, as

noted supra, does not recognize that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to transdermal delivery.

With regard to the rejection based on the combined teachings of Sebel, Tyle, Banga and Ariura, none of the references applied in this rejection teaches that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to iontophoretic delivery. While Sebel recognizes that fentanyl possesses properties making it susceptible to transdermal delivery, this reference does not recognize that fentanyl also possesses properties making it susceptible to iontophoretic delivery. This deficiency of Sebel is not rectified by the collective teachings of Tyle, Banga and Ariura for reasons stated supra.

With regard to the rejection based on Sasaki and Yamanaka, neither of these references contains a teaching that fentanyl or any of the other drugs recited in the above-mentioned Markush group has properties making it susceptible to iontophoretic or transdermal delivery.

In addition to the forgoing shortcomings of the cited references as applied by the examiner, we cannot ignore the

declaration evidence, particularly the Haak and Cormier declarations, concerning the unpredictable nature of fentanyl and fentanyl salts. In particular, Haak states in paragraph 4 that "a person skilled in the art . . . would not be certain that fentanyl salts which have lower aqueous solubility than any of the drugs listed in Table 1, could be delivered transdermally by electrotransport at therapeutically effective rates" (emphasis in the original). Reinforcing his assertion of uncertainty, Haak states in paragraph 10 that in his opinion, "one cannot simply substitute a drug described to be delivered by the microiontophoresis technique and expect that the same drug will be deliverable, at therapeutic levels and by means of devices of workable size, by transdermal iontophoresis."

The Cormier declaration emphasizes the uncertainty of delivering fentanyl transdermally by iontophoresis without skin irritation. In particular, Cormier states in paragraph 9 that "even though passive fentanyl delivery was known not to cause significant skin irritation, before attempting to deliver fentanyl transdermally [by] electrotransport, persons skilled in the electrotransport art would not have been

certain that transdermal electrotransport fentanyl delivery could be accomplished without causing skin irritation . . .” (emphasis in the original). In view of the Cormier declaration, appellant asserts on page 34 of the main brief that “lack of skin irritation was not predictable” (emphasis added).

The examiner has proffered no evidence to rebut the forgoing declaration evidence.

For the foregoing reasons, the examiner's decision rejecting the appealed claims is reversed.

REVERSED

HARRISON E. McCANDLISH, Senior Administrative Patent Judge	)	
LAWRENCE J. STAAB Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
JOHN P. McQUADE Administrative Patent Judge	)	

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